

Appln. No. 10/600,695
Response dated September 19, 2005
Reply to Office Action dated May 19, 2005

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1. - 20. (Canceled)

21. (Currently amended) A pharmaceutical composition for preventing ~~or treating~~ a condition in a mammal characterized by undesired thrombosis comprising a pharmaceutically acceptable carrier and a pharmaceutically effective amount of a compound of ~~claim 1~~ the formula (I):

A-Q-D-E-G-J-X

wherein:

A is selected from the group consisting of:

-C(=NR²)N(R²,R³); and

phenyl, which is substituted with 0-2 R¹ groups;

each R¹ is a member independently selected from the group consisting of:

halo, -CN, -C(=O)-N(R², R³), -NO₂, -SO₂N(R², R³), -SO₂R², -(CH₂)_mNR²R³, -(CH₂)_m-C(=NR³)-R², -(CH₂)_m-C(=NR²)-N(R²,R³), -(CH₂)_m-N(R²)-C(=NR²)-N(R²,R³), -(CH₂)_mNR²-C₃₋₆heterocyclics, C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₈cycloalkyl, C₀₋₄alkylC₃₋₈cycloalkyl, -CF₃, -OR², and a 5-6 membered heterocyclic system containing from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic system may be independently replaced with a member selected from the group consisting of halo, C₁-C₄-alkyl, -CN, C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₈cycloalkyl, C₀₋₄alkylC₃₋₈cycloalkyl and -NO₂;

each R² and R³ is a member independently selected from the group consisting of:

-H, -C₁₋₆alkyl, -C₁₋₆alkyloxy, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₆alkylC₃₋₈cycloalkyl and -C₀₋₆alkyl-(carbocyclic aryl), wherein from 0-4 hydrogen atoms on the ring atoms of the carbocyclic aryl moiety may be independently replaced with a member selected from the group consisting of halo, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -S(=O)₂-OH, -CN, -CF₃ and -NO₂;

m is an integer of 0-2;

Q is a direct link;

D is phenyl, which is substituted with 0-2 R^{1a} groups;

each R^{1a} is a member independently selected from the group consisting of:

halo, -C₁₋₆alkyl, -C₁₋₆alkyloxy, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₆alkylC₃₋₈cycloalkyl, -S(=O)₂-OH, -CN, -NO₂, -(CH₂)_n-N(-R^{2a}, -R^{3a}), -S(=O)₂-N(-R^{2a}, -R^{3a}), -S(=O)₂-R^{2a}, -CF₃, -(CH₂)_n-OR^{2a}, -C(=O)-O-R^{2a}, -C(=O)-N(-R^{2a}, -R^{3a}), -C(=NH)-N(-R^{2a}, -R^{3a}), -C(=NMe)-N(-R^{2a}, -R^{3a}), 2-imidazolin-2-yl, 1-methyl-2-imidazolin-2-yl and a 5-6 membered aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S and -C₀₋₆alkyl-(carbocyclic aryl), wherein from 0-4 hydrogen atoms on the ring atoms of the aromatic heterocyclic ring and the carbocyclic aryl moiety may be independently replaced with a member selected from the group consisting of halo, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -CN, -CF₃ and -NO₂;

n is an integer of 0-2;

R^{2a} and R^{3a} are independently selected from the group consisting of:

-H, -C₁₋₆alkyl, -C₁₋₆alkyloxy, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₆alkylC₃₋₈cycloalkyl and -C₀₋₆alkyl-(carbocyclic aryl), wherein from 0-4 hydrogen atoms on the ring atoms of the carbocyclic aryl moiety may be independently replaced with a member selected from the group consisting of halo,

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-C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl,
-S(=O)₂-OH, -CN, -CF₃ and -NO₂;

E is -NH-C(=O)-;

G is a pyrazole ring substituted with 0-2 R^{1b} groups;

each R^{1b} is a member independently selected from the group consisting of:

halo, -C₁₋₆alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₆alkylC₃₋₈cycloalkyl,
-C₁₋₄alkyl-C(=O)-OH, -CN, -NO₂, -S(=O)₂-OH, -N(-R^{2b}, -R^{3b}), -C(=O)-N(-R^{2b}, -R^{3b}), -
S(=O)₂-N(-R^{2b}, -R^{3b}), -S(=O)₂-R^{2b}, -CF₃, -O-R^{2b}, -O-CH₂-CH₂-O-R^{2b},
-O-CH₂-C(=O)-O-R^{2b}, -N(-R^{2b})-CH₂-CH₂-O-R^{2b}, -N(-CH₂-CH₂-O-R^{2b})₂,
-N(-R^{2b})-C(=O)-R^{3b}, -N(-R^{2b})-S(=O)₂-R^{3b}, and a 5-6 membered heterocyclic ring
containing 1-4 heteroatoms selected from N, O and S substituted with 0-4 R^{1b}
groups;

each R^{2b} and R^{3b} is a member independently selected from the group consisting of:

-H, -C₁₋₆alkyl, -C₁₋₆alkyloxy, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl,
-C₀₋₆alkylC₃₋₈cycloalkyl and -C₀₋₆alkyl-(carbocyclic aryl), wherein from 0-4
hydrogen atoms on the ring atoms of the carbocyclic aryl moiety may be
independently replaced with a member selected from the group consisting of halo, -
C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -
S(=O)₂-O⁻, -CN, -CF₃ and -NO₂;

each R^{1b'} is a member independently selected from the group consisting of:

halo, -C₁₋₆alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₆alkylC₃₋₈cycloalkyl,
-C₁₋₄alkyl-C(=O)-OH, -CN, -NO₂, -S(=O)₂-OH, -N(-R^{2b'}, -R^{3b'}), -C(=O)-N(-R^{2b'}, -
R^{3b'}), -S(=O)₂-N(-R^{2b'}, -R^{3b'}), -S(=O)₂-R^{2b'}, -CF₃, -O-R^{2b'}, -O-CH₂-CH₂-O-R^{2b'},
-O-CH₂-C(=O)-O-R^{2b'}, -N(-R^{2b'})-CH₂-CH₂-O-R^{2b'}, -N(-CH₂-CH₂-O-R^{2b'})₂,
-N(-R^{2b'})-C(=O)-R^{3b'} and -N(-R^{2b'})-S(=O)₂-R^{3b'};

each $R^{2b'}$ and $R^{3b'}$ are independently selected from the group consisting of:

-H, -C₁₋₆alkyl, -C₁₋₆alkoxy, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₆alkylC₃₋₈cycloalkyl and -C₀₋₆alkyl-(carbocyclic aryl), wherein from 0-4 hydrogen atoms on the ring atoms of the carbocyclic aryl moiety may be independently replaced with a member selected from the group consisting of halo, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -S(=O)₂-OH, -CN, -CF₃ and -NO₂;

J is a direct link;

X is a naphthyl, which is substituted with 0-3 R^{1c} groups;

each R^{1c} is a member independently selected from the group consisting of:

halo, -CF₃, -C₁₋₆alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₆alkylC₃₋₈cycloalkyl, -C₁₋₄alkyl-C(=O)-OH, -CF₃, -CN, -NO₂, -(CH₂)_z-N(-R^{2c}, -R^{3c}), -C(=O)-N(-R^{2c}, -R^{3c}), -C(=NH)-N(-R^{2c}, -R^{3c}), -C(=NMe)-N(-R^{2c}, -R^{3c}), -S(=O)₂-N(-R^{2c}, -R^{3c}), -S(=O)₂-R^{2c}, -S(=O)₂-OH, -CF₃, -O-R^{2c}, -O-(CH₂)_z-O-R^{2c}, -O-(CH₂)_z-C(=O)-O-R^{2c}, -N(-R^{2c}), -O-(CH₂)_z-O-R^{2c}, -N[-(CH₂)_z-O-R^{2c}]₂, -(CH₂)_z-N(-R^{2c})-C(=O)-R^{3c}, -(CH₂)_z-N(-R^{2c})-S(=O)₂-R^{3c}, and a 5-6 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

z is an integer of 0-4;

each R^{2c} and R^{3c} is a member independently selected from the group consisting of:

-H, -C₁₋₆alkyl, -C₁₋₆alkoxy, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₆alkylC₃₋₈cycloalkyl and -C₀₋₆alkyl-(carbocyclic aryl), wherein from 0-4 hydrogen atoms on the ring atoms of the carbocyclic aryl moiety may be independently replaced with a member selected from the group consisting of halo, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -S(=O)₂-OH, -CN, -CF₃ and -NO₂;

and all pharmaceutically acceptable diastereomers, enantiomers or mixtures thereof, salts, hydrates or solvates thereof.

22. (Currently amended) A method for preventing ~~or treating~~ a condition in a mammal characterized by undesired thrombosis comprising administering to said mammal a therapeutically effective amount of a compound of ~~claim 1~~ the formula (I):

A-Q-D-E-G-J-X

wherein:

A is selected from the group consisting of:

-C(=NR²)N(R²,R³); and

phenyl, which is substituted with 0-2 R¹ groups;

each R¹ is a member independently selected from the group consisting of:

halo, -CN, -C(=O)-N(R², R³), -NO₂, -SO₂N(R², R³), -SO₂R², -(CH₂)_mNR²R³, -(CH₂)_m-C(=NR³)-R², -(CH₂)_m-C(=NR²)-N(R²,R³), -(CH₂)_m-N(R²)-C(=NR²)-N(R²,R³), -(CH₂)_mNR²-C₃₋₆heterocyclics, C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₈cycloalkyl, C₀₋₄alkylC₃₋₈cycloalkyl, -CF₃, -OR², and a 5-6 membered heterocyclic system containing from 1-4 heteroatoms selected from N, O and S, wherein from 1-4 hydrogen atoms on the heterocyclic system may be independently replaced with a member selected from the group consisting of halo, C₁₋₄alkyl, -CN C₁₋₄alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₈cycloalkyl, C₀₋₄alkylC₃₋₈cycloalkyl and -NO₂;

each R² and R³ is a member independently selected from the group consisting of:

-H, -C₁₋₆alkyl, -C₁₋₆alkyloxy, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₆alkylC₃₋₈cycloalkyl and -C₀₋₆alkyl-(carbocyclic aryl), wherein from 0-4 hydrogen atoms on the ring atoms of the carbocyclic aryl moiety may be independently replaced with a member selected from the group consisting of halo, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -S(=O)₂-OH, -CN, -CF₃ and -NO₂;

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m is an integer of 0-2;

Q is a direct link;

D is phenyl, which is substituted with 0-2 R^{1a} groups;

each R^{1a} is a member independently selected from the group consisting of:

halo, -C₁₋₆alkyl, -C₁₋₆alkyloxy, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₆alkylC₃₋₈cycloalkyl, -S(=O)₂-OH, -CN, -NO₂, -(CH₂)_n-N(-R^{2a}, -R^{3a}), -S(=O)₂-N(-R^{2a}, -R^{3a}), -S(=O)₂-R^{2a}, -CF₃, -(CH₂)_n-OR^{2a}, -C(=O)-O-R^{2a}, -C(=O)-N(-R^{2a}, -R^{3a}), -C(=NH)-N(-R^{2a}, -R^{3a}), -C(=NMe)-N(-R^{2a}, -R^{3a}), 2-imidazolin-2-yl, 1-methyl-2-imidazolin-2-yl and a 5-6 membered aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S and -C₀₋₆alkyl-(carbocyclic aryl), wherein from 0-4 hydrogen atoms on the ring atoms of the aromatic heterocyclic ring and the carbocyclic aryl moiety may be independently replaced with a member selected from the group consisting of halo, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -CN, -CF₃ and -NO₂;

n is an integer of 0-2;

R^{2a} and R^{3a} are independently selected from the group consisting of:

-H, -C₁₋₆alkyl, -C₁₋₆alkyloxy, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₆alkylC₃₋₈cycloalkyl and -C₀₋₆alkyl-(carbocyclic aryl), wherein from 0-4 hydrogen atoms on the ring atoms of the carbocyclic aryl moiety may be independently replaced with a member selected from the group consisting of halo, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -S(=O)₂-OH, -CN, -CF₃ and -NO₂;

E is -NH-C(=O)-;

G is a pyrazole ring substituted with 0-2 R^{1b} groups;

each R^{1b} is a member independently selected from the group consisting of:

halo, -C₁₋₆alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₆alkylC₃₋₈cycloalkyl, -C₁₋₄alkyl-C(=O)-OH, -CN, -NO₂, -S(=O)₂-OH, -N(-R^{2b}, -R^{3b}), -C(=O)-N(-R^{2b}, -R^{3b}), -S(=O)₂-N(-R^{2b}, -R^{3b}), -S(=O)₂-R^{2b}, -CF₃, -O-R^{2b}, -O-CH₂-CH₂-O-R^{2b}, -O-CH₂-C(=O)-O-R^{2b}, -N(-R^{2b})-CH₂-CH₂-O-R^{2b}, -N(-CH₂-CH₂-O-R^{2b})₂, -N(-R^{2b})-C(=O)-R^{3b}, -N(-R^{2b})-S(=O)₂-R^{3b}, and a 5-6 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S substituted with 0-4 R^{1b'} groups;

each R^{2b} and R^{3b} is a member independently selected from the group consisting of:

-H, -C₁₋₆alkyl, -C₁₋₆alkyloxy, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₆alkylC₃₋₈cycloalkyl and -C₀₋₆alkyl-(carbocyclic aryl), wherein from 0-4 hydrogen atoms on the ring atoms of the carbocyclic aryl moiety may be independently replaced with a member selected from the group consisting of halo, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -S(=O)₂-O⁻, -CN, -CF₃ and -NO₂;

each R^{1b'} is a member independently selected from the group consisting of:

halo, -C₁₋₆alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₆alkylC₃₋₈cycloalkyl, -C₁₋₄alkyl-C(=O)-OH, -CN, -NO₂, -S(=O)₂-OH, -N(-R^{2b'}, -R^{3b'}), -C(=O)-N(-R^{2b'}, -R^{3b'}), -S(=O)₂-N(-R^{2b'}, -R^{3b'}), -S(=O)₂-R^{2b'}, -CF₃, -O-R^{2b'}, -O-CH₂-CH₂-O-R^{2b'}, -O-CH₂-C(=O)-O-R^{2b'}, -N(-R^{2b'})-CH₂-CH₂-O-R^{2b'}, -N(-CH₂-CH₂-O-R^{2b'})₂, -N(-R^{2b'})-C(=O)-R^{3b'} and -N(-R^{2b'})-S(=O)₂-R^{3b'};

each R^{2b'} and R^{3b'} are independently selected from the group consisting of:

-H, -C₁₋₆alkyl, -C₁₋₆alkoxy, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₆alkylC₃₋₈cycloalkyl and -C₀₋₆alkyl-(carbocyclic aryl), wherein from 0-4 hydrogen atoms on the ring atoms of the carbocyclic aryl moiety may be independently replaced with a member selected from the group consisting of halo, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -S(=O)₂-OH, -CN, -CF₃ and -NO₂;

J is a direct link;

X is a naphthyl, which is substituted with 0-3 R^{1c} groups;

each R^{1c} is a member independently selected from the group consisting of:

halo, -CF₃, -C₁₋₆alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₆alkylC₃₋₈cycloalkyl, -C₁₋₄alkyl-C(=O)-OH, -CF₃, -CN, -NO₂, -(CH₂)_z-N(-R^{2c}, -R^{3c}), -C(=O)-N(-R^{2c}, -R^{3c}), -C(=NH)-N(-R^{2c}, -R^{3c}), -C(=NMe)-N(-R^{2c}, -R^{3c}), -S(=O)₂-N(-R^{2c}, -R^{3c}), -S(=O)₂-R^{2c}, -S(=O)₂-OH, -CF₃, -O-R^{2c}, -O-(CH₂)_z-O-R^{2c}, -O-(CH₂)_z-C(=O)-O-R^{2c}, -N(-R^{2c}), -O-(CH₂)_z-O-R^{2c}, -N[(CH₂)_z-O-R^{2c}]₂, -(CH₂)_z-N(-R^{2c})-C(=O)-R^{3c}, -(CH₂)_z-N(-R^{2c})-S(=O)₂-R^{3c}, and a 5-6 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

z is an integer of 0-4;

each R^{2c} and R^{3c} is a member independently selected from the group consisting of:

-H, -C₁₋₆alkyl, -C₁₋₆alkyloxy, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₆alkylC₃₋₈cycloalkyl and -C₀₋₆alkyl-(carbocyclic aryl), wherein from 0-4 hydrogen atoms on the ring atoms of the carbocyclic aryl moiety may be independently replaced with a member selected from the group consisting of halo, -C₁₋₄alkyl, -C₂₋₆alkenyl, -C₂₋₆alkynyl, -C₃₋₈cycloalkyl, -C₀₋₄alkylC₃₋₈cycloalkyl, -S(=O)₂-OH, -CN, -CF₃ and -NO₂;

and all pharmaceutically acceptable diastereomers, enantiomers or mixtures thereof, salts, hydrates or solvates thereof.

23. (Currently amended) The method of claim **22 6**, wherein the condition is selected from the group consisting of:

acute coronary syndrome, myocardial infarction, unstable angina, refractory angina, occlusive coronary thrombus occurring post-thrombolytic therapy or post-coronary angioplasty, a thrombotically mediated cerebrovascular syndrome, embolic stroke, thrombotic stroke, transient ischemic attacks, venous thrombosis, deep venous

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thrombosis, pulmonary embolus, coagulopathy, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, thromboangiitis obliterans, thrombotic disease associated with heparin-induced thrombocytopenia, thrombotic complications associated with extracorporeal circulation, thrombotic complications associated with instrumentation, and thrombotic complications associated with the fitting of prosthetic devices.

24. (Canceled)

25. (Currently amended) A pharmaceutical composition of claim 21 for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising a pharmaceutically acceptable carrier and a pharmaceutically effective amount of a compound of claim 2

wherein:

A is phenyl, which is substituted with 0-2 R¹ groups;

each R¹ is a member independently selected from the group consisting of:

halo, C₁₋₄alkyl, -CN, -C(=O)-N(R², R³), -NO₂, -SO₂N(R², R³), -SO₂R², -(CH₂)_mNR²R³, -(CH₂)_m-C(=NR³)-R², -(CH₂)_m-C(=NR²)-N(R², R³), -(CH₂)_m-N(R²)-C(=NR²)-N(R², R³), -(CH₂)_mNR²-C₃₋₆heterocyclics, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₈cycloalkyl, C₀₋₄alkylC₃₋₈cycloalkyl, -CF₃, -OR², and a 5-6 membered heterocyclic system containing from 1-4 heteroatoms selected from N, O and S;

each R² and R³ is a member independently selected from the group consisting of:

-H, -C₁₋₄alkyl and -C₀₋₄alkyl-(carbocyclic aryl);

m is an integer of 0-2;

Q is a direct link;

D is phenyl, which is substituted with 0-2 R^{1a} groups;

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each R^{1a} is a member independently selected from the group consisting of:

halo, -C₁₋₄alkyl, -CN, -NO₂, -(CH₂)_n-N(-R^{2a}, -R^{3a}), -S(=O)₂-N(-R^{2a}, -R^{3a}), -S(=O)₂-R^{2a}, -CF₃, -(CH₂)_n-OR^{2a}, -C(=O)-O-R^{2a}, -C(=O)-N(-R^{2a}, -R^{3a}), and a 5-6 membered aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

n is an integer of 0-2;

R^{2a} and R^{3a} are independently selected from the group consisting of:

-H, -C₁₋₄alkyl and -C₁₋₄alkyl-(carbocyclic aryl);

E is -NH-C(=O)-;

G is a pyrazole ring substituted with 0-2 R^{1b} groups;

each R^{1b} is a member independently selected from the group consisting of:

halo, -C₁₋₄alkyl, -CN, -NO₂, -N(-R^{2b}, -R^{3b}), -C(=O)-N(-R^{2b}, -R^{3b}), -S(=O)₂-N(-R^{2b}, -R^{3b}), -S(=O)₂-R^{2b}, -CF₃, -O-R^{2b}, -O-CH₂-CH₂-O-R^{2b}, -O-CH₂-C(=O)-O-R^{2b}, -N(-R^{2b})-CH₂-CH₂-O-R^{2b}, -N(-CH₂-CH₂-O-R^{2b})₂, -N(-R^{2b})-C(=O)-R^{3b}, -N(-R^{2b})-S(=O)₂-R^{3b}, and a 5-6 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

each R^{2b} and R^{3b} is a member independently selected from the group consisting of:

-H, -C₁₋₄alkyl and -C₁₋₄alkyl-(carbocyclic aryl);

J is a direct link;

X is a naphthyl, which is substituted with 0-3 R^{1c} groups;

each R^{1c} is a member independently selected from the group consisting of:

halo, -C₁₋₄alkyl, -CN, -NO₂, -(CH₂)₂-N(-R^{2c}, -R^{3c}), -C(=O)-N(-R^{2c}, -R^{3c}), -C(=NH)-N(-R^{2c}, -R^{3c}), -C(=NMe)-N(-R^{2c}, -R^{3c}), -S(=O)₂-N(-R^{2c}, -R^{3c}), -S(=O)₂-R^{2c},

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$-S(=O)_2-OH$, $-CF_3$, $-O-R^{2c}$, $-O-(CH_2)_z-O-R^{2c}$, $-O-(CH_2)_z-C(=O)-O-R^{2c}$, $-N(-R^{2c})$,
 $-O-(CH_2)_z-O-R^{2c}$, $-N[(CH_2)_z-O-R^{2c}]_2$, $-(CH_2)_z-N(-R^{2c})-C(=O)-R^{3c}$,
 $-(CH_2)_z-N(-R^{2c})-S(=O)_2-R^{3c}$, and a 5-6 membered heterocyclic ring containing 1-4
heteroatoms selected from N, O and S;

z is an integer of 0-4;

each R^{2c} and R^{3c} is a member independently selected from the group consisting of:

$-H$, $-C_{1-4}alkyl$ and $-C_{1-4}alkyl-(carbocyclic\ aryl)$;

or all pharmaceutically acceptable diastereomers, enantiomers or mixtures thereof, salts, hydrates or solvates thereof.

26. (Currently amended) ~~The A method for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising administering to said mammal a therapeutically effective amount of a compound of claim 2~~ 22

wherein:

A is selected from the group consisting of:

phenyl, which is substituted with 0-2 R^1 groups;

each R^1 is a member independently selected from the group consisting of:

halo, $C_{1-4}alkyl$, $-CN$, $-C(=O)-N(R^2, R^3)$, $-NO_2$, $-SO_2N(R^2, R^3)$, $-SO_2R^2$, $-(CH_2)_mNR^2R^3$,
 $-(CH_2)_m-C(=NR^3)-R^2$, $-(CH_2)_m-C(=NR^2)-N(R^2, R^3)$, $-(CH_2)_m-N(R^2)-C(=NR^2)-N(R^2, R^3)$,
 $-(CH_2)_mNR^2-C_{3-6}heterocyclics$, $C_{2-6}alkenyl$, $C_{2-6}alkynyl$, $C_{3-8}cycloalkyl$, $C_{0-4}alkylC_{3-8}cycloalkyl$, $-CF_3$, $-OR^2$, and a 5-6 membered heterocyclic system containing from 1-4 heteroatoms selected from N, O and S;

each R^2 and R^3 is a member independently selected from the group consisting of:

$-H$, $-C_{1-4}alkyl$ and $-C_{0-4}alkyl-(carbocyclic\ aryl)$;

m is an integer of 0-2;

Q is a direct link;

D is phenyl, which is substituted with 0-2 R^{1a} groups;

each R^{1a} is a member independently selected from the group consisting of:

halo, -C₁₄alkyl, -CN, -NO₂, -(CH₂)_n-N(-R^{2a}, -R^{3a}), -S(=O)₂-N(-R^{2a}, -R^{3a}), -S(=O)₂-R^{2a},
-CF₃, -(CH₂)_n-OR^{2a}, -C(=O)-O-R^{2a}, -C(=O)-N(-R^{2a}, -R^{3a}), and a 5-6 membered
aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

n is an integer of 0-2;

R^{2a} and R^{3a} are independently selected from the group consisting of:

-H, -C₁₋₄alkyl and -C₁₋₄alkyl-(carbocyclic aryl);

E is -NH-C(=O)-;

G is a pyrazole ring substituted with 0-2 R^{1b} groups;

each R^{1b} is a member independently selected from the group consisting of:

halo, -C₁₋₄alkyl, -CN, -NO₂, -N(-R^{2b}, -R^{3b}), -C(=O)-N(-R^{2b}, -R^{3b}), -S(=O)₂-N(-R^{2b}, -
R^{3b}), -S(=O)₂-R^{2b}, -CF₃, -O-R^{2b}, -O-CH₂-CH₂-O-R^{2b}, -O-CH₂-C(=O)-O-R^{2b},
-N(-R^{2b})-CH₂-CH₂-O-R^{2b}, -N(-CH₂-CH₂-O-R^{2b})₂, -N(-R^{2b})-C(=O)-R^{3b},
-N(-R^{2b})-S(=O)₂-R^{3b}, and a 5-6 membered heterocyclic ring containing 1-4
heteroatoms selected from N, O and S;

each R^{2b} and R^{3b} is a member independently selected from the group consisting of:

-H, -C₁₋₄alkyl and -C₁₋₄alkyl-(carbocyclic aryl);

J is a direct link;

X is a naphthyl, which is substituted with 0-3 R^{1c} groups;

each R^{1c} is a member independently selected from the group consisting of:

halo, -C₁₋₄alkyl, -CN, -NO₂, -(CH₂)_z-N(-R^{2c}, -R^{3c}), -C(=O)-N(-R^{2c}, -R^{3c}),
-C(=NH)-N(-R^{2c}, -R^{3c}), -C(=NMe)-N(-R^{2c}, -R^{3c}), -S(=O)₂-N(-R^{2c}, -R^{3c}), -S(=O)₂-R^{2c},
-S(=O)₂-OH, -CF₃, -O-R^{2c}, -O(-CH₂)_z-O-R^{2c}, -O(-CH₂)_z-C(=O)-O-R^{2c}, -N(-R^{2c}),
-O(-CH₂)_z-O-R^{2c}, -N[(-CH₂)_z-O-R^{2c}]₂, -(CH₂)_z-N(-R^{2c})-C(=O)-R^{3c},
-(CH₂)_z-N(-R^{2c})-S(=O)₂-R^{3c}, and a 5-6 membered heterocyclic ring containing 1-4
heteroatoms selected from N, O and S;

z is an integer of 0-4;

each R^{2c} and R^{3c} is a member independently selected from the group consisting of:

-H, -C₁₋₄alkyl and -C₁₋₄alkyl-(carbocyclic aryl);

or all pharmaceutically acceptable diastereomers, enantiomers or mixtures thereof, salts, hydrates or solvates thereof.

27. (Currently amended) The method of claim ~~26~~ 10, wherein the condition is selected from the group consisting of:

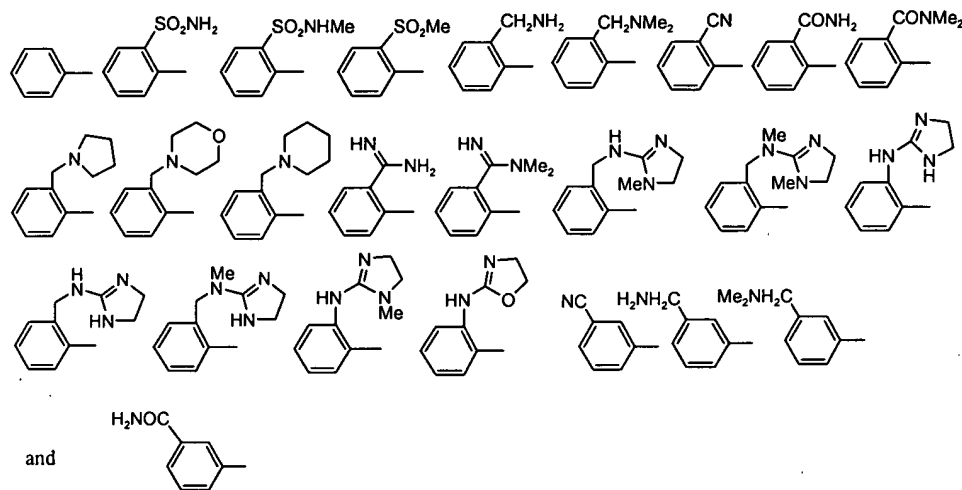
acute coronary syndrome, myocardial infarction, unstable angina, refractory angina, occlusive coronary thrombus occurring post-thrombolytic therapy or post-coronary angioplasty, a thrombotically mediated cerebrovascular syndrome, embolic stroke, thrombotic stroke, transient ischemic attacks, venous thrombosis, deep venous thrombosis, pulmonary embolus, coagulopathy, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, thromboangiitis obliterans, thrombotic disease associated with heparin-induced thrombocytopenia, thrombotic complications associated with extracorporeal circulation, thrombotic complications associated with instrumentation, and thrombotic complications associated with the fitting of prosthetic devices.

28. (Canceled)

29. (Currently amended) A pharmaceutical composition of claim 21 for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising a pharmaceutically acceptable carrier and a pharmaceutically effective amount of a compound of claim 3

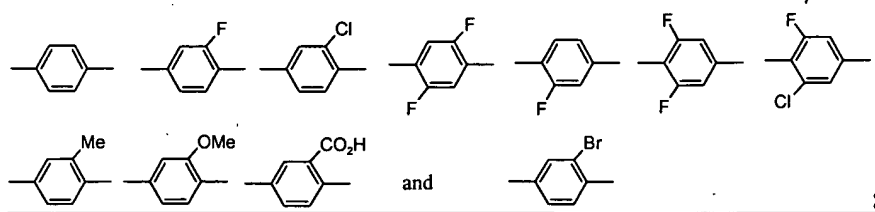
wherein:

A is selected from the group consisting of:



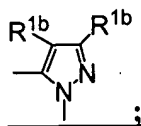
Q is a direct link;

D is selected from the group consisting of:



E is -NH-C(=O)-;

G has the following formula:



each R^{1b} is a member independently selected from the group consisting of:

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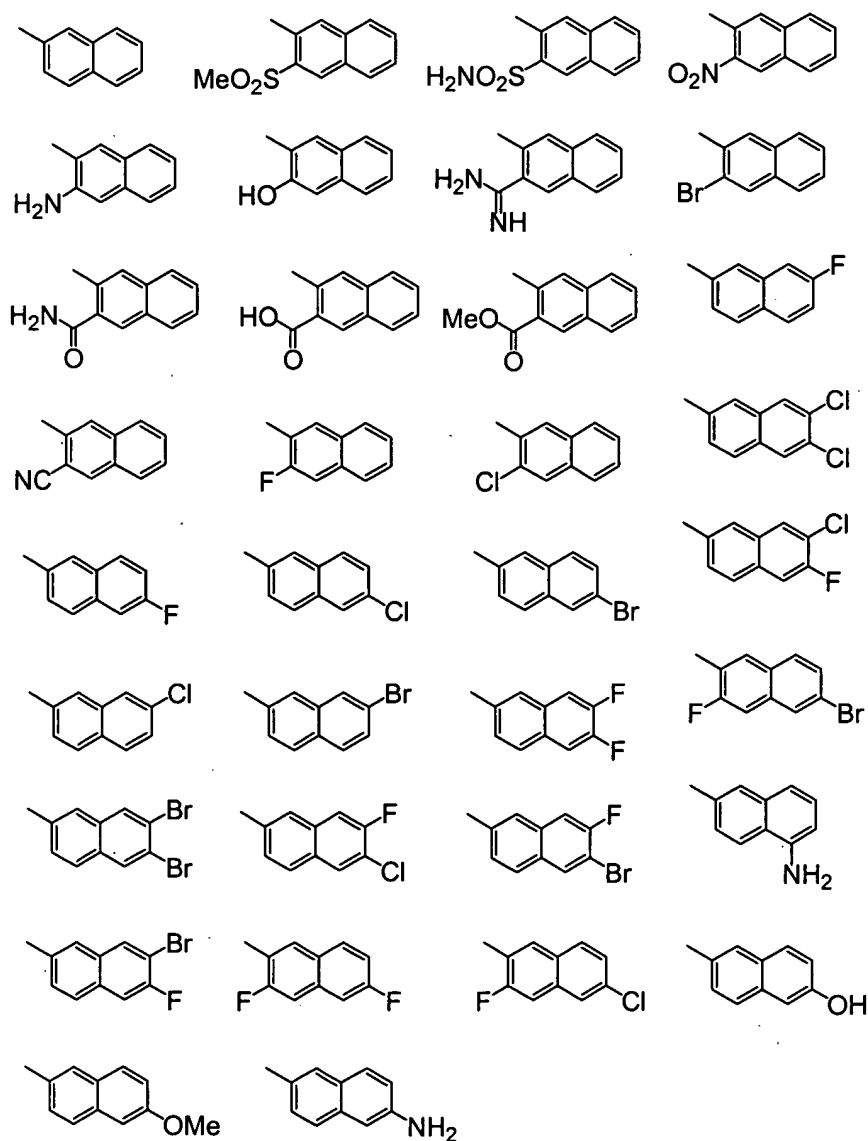
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-H, -Me, -CF₃, -F, -Cl, -Br, -SO₂Me, -CN, -CONH₂, -CONMe₂, -NH₂, -NO₂, -NHCOMe, -NHSO₂Me, -CH₂NH₂ and -CO₂H;

J is a direct link;

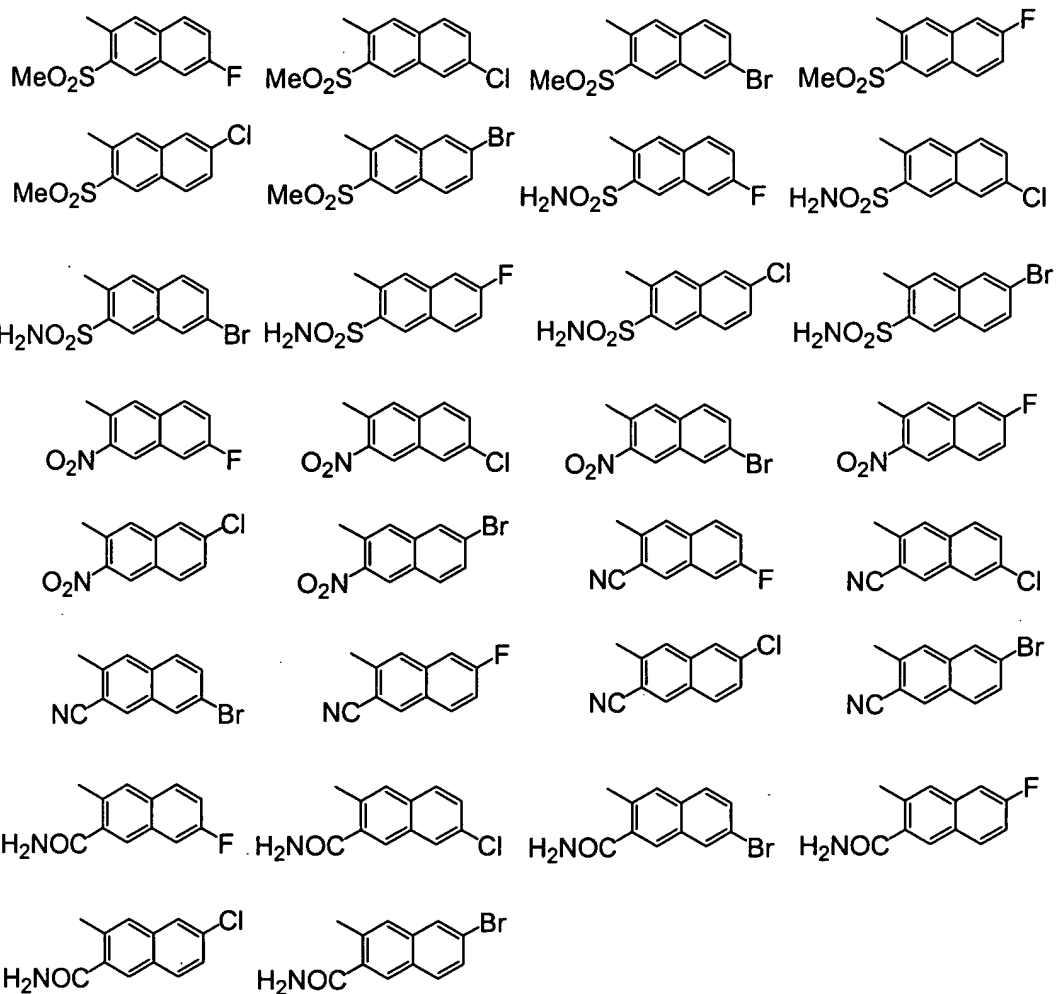
X is selected from the group consisting of:

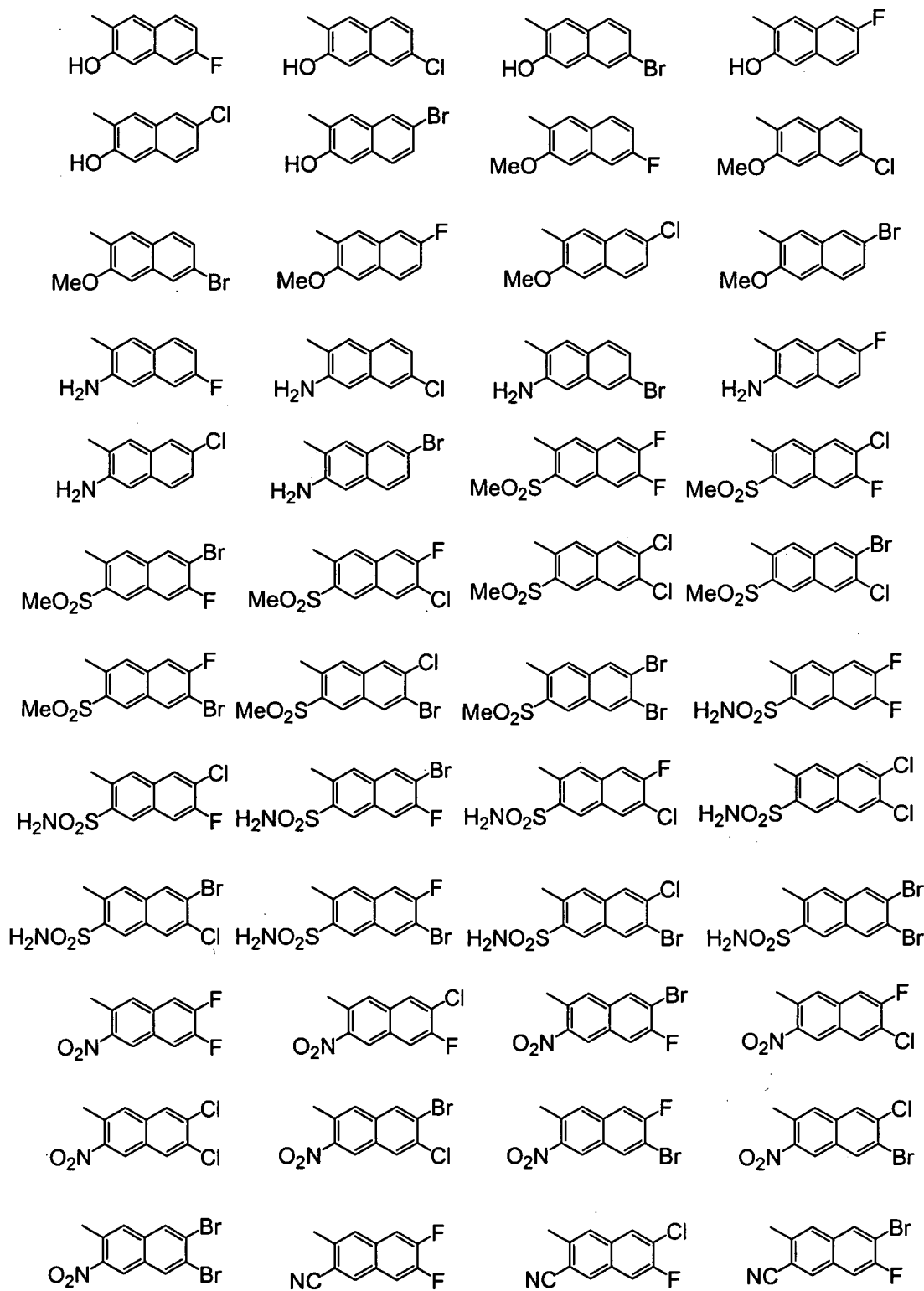


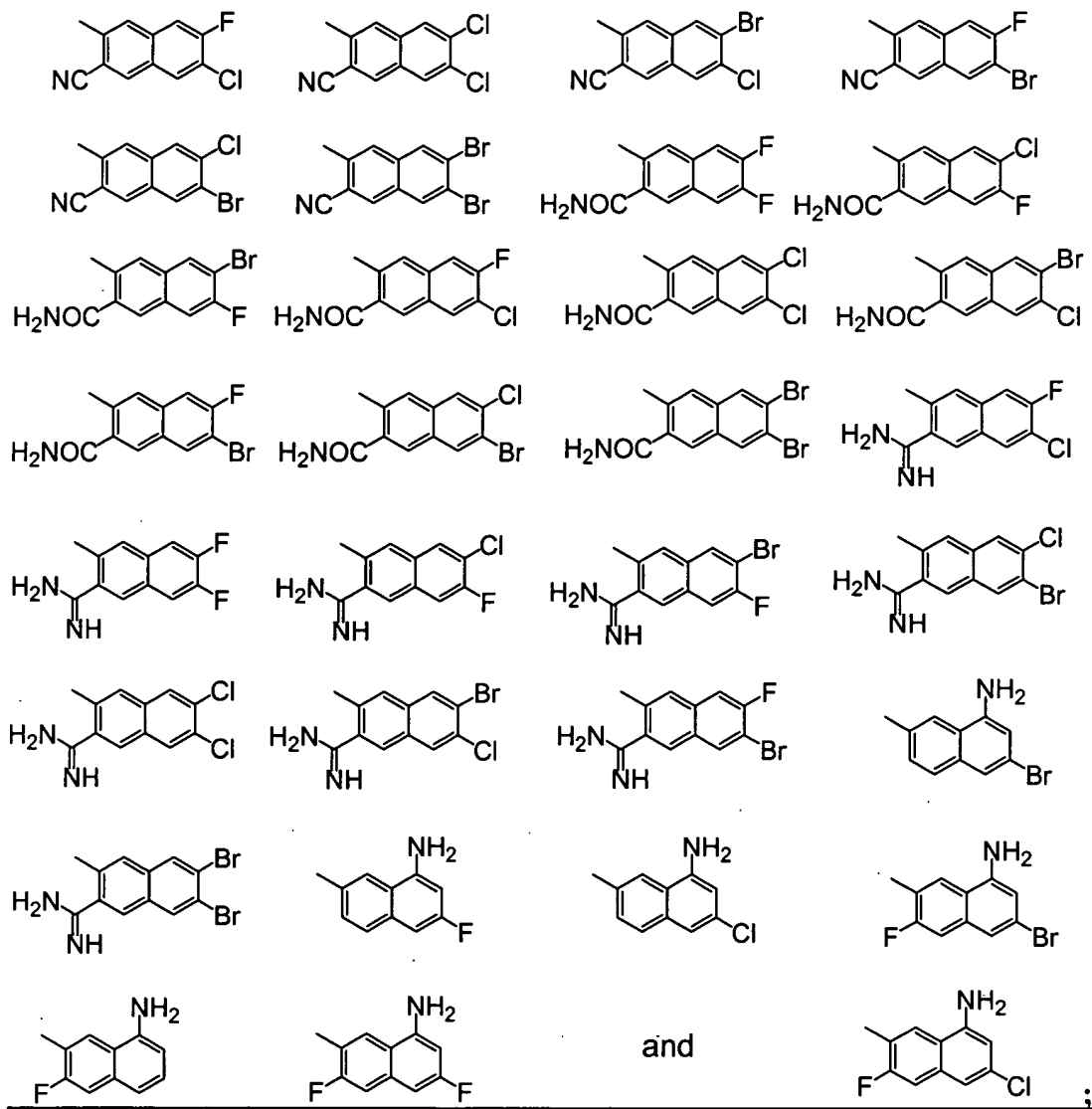
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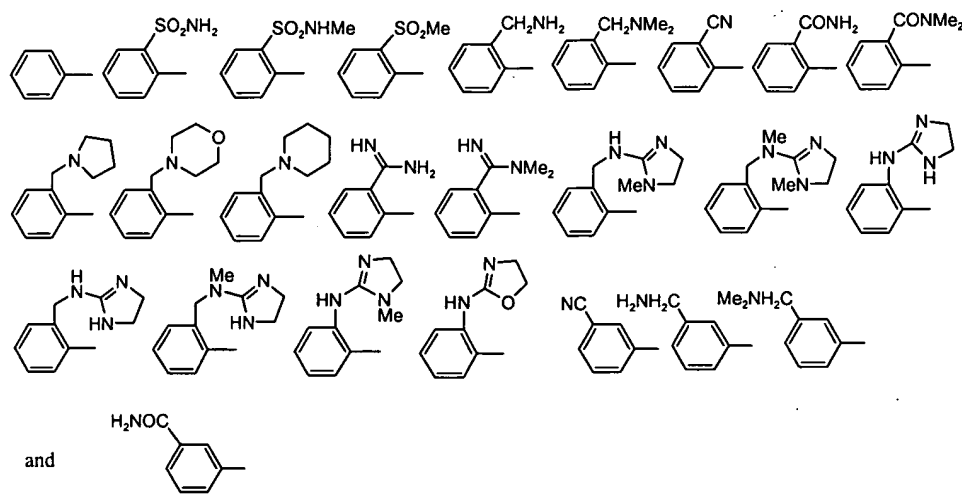
or all pharmaceutically acceptable diastereomers, enantiomers or mixtures thereof, salts, hydrates or solvates thereof

30. (Currently amended) ~~The A method for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising administering to said mammal a therapeutically effective amount of a compound~~ of claim-3 22

wherein:

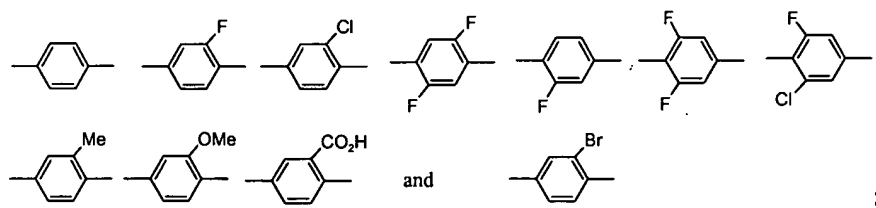
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A is selected from the group consisting of:



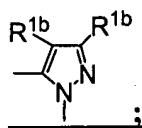
Q is a direct link;

D is selected from the group consisting of:



E is -NH-C(=O)-;

G has the following formula:



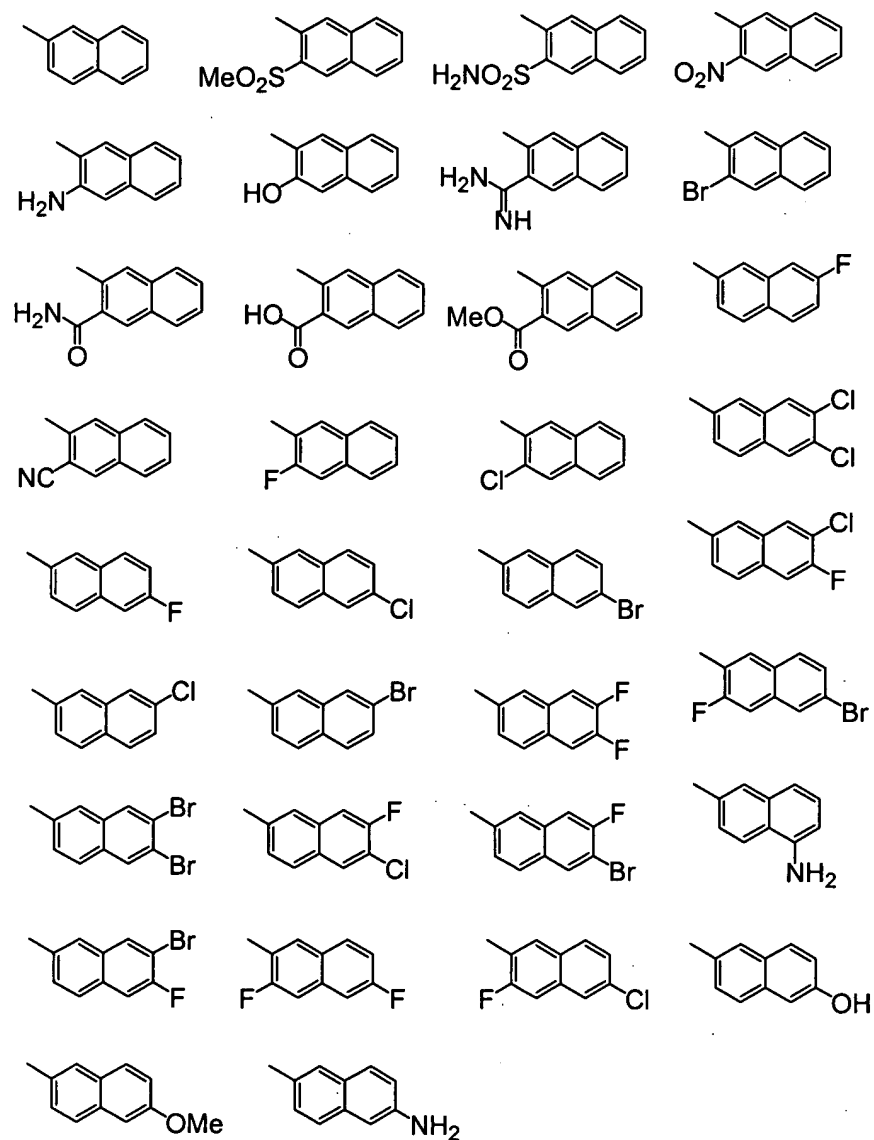
each R^{1b} is a member independently selected from the group consisting of:

-H, -Me, -CF₃, -F, -Cl, -Br, -SO₂Me, -CN, -CONH₂, -CONMe₂, -NH₂, -NO₂, -NHCOMe, -NHSO₂Me, -CH₂NH₂ and -CO₂H;

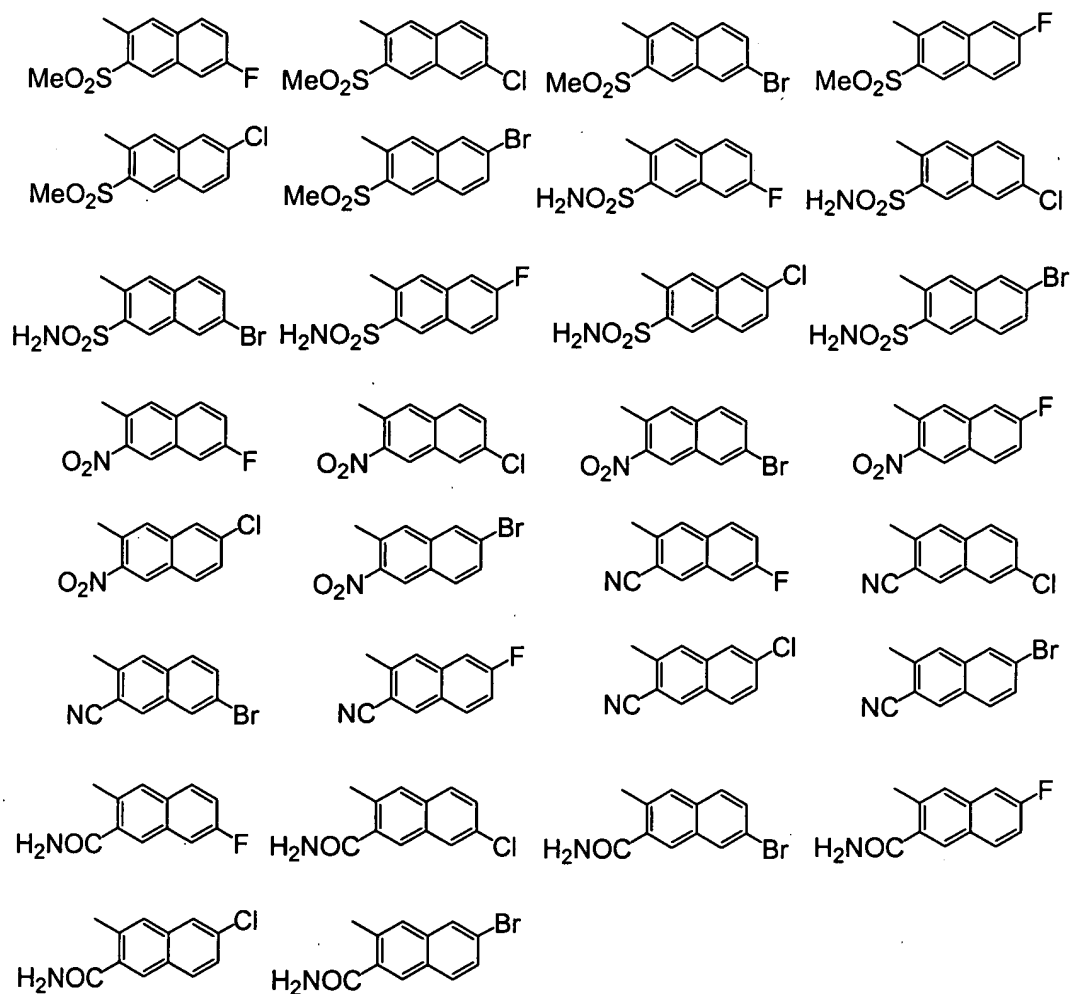
J is a direct link;

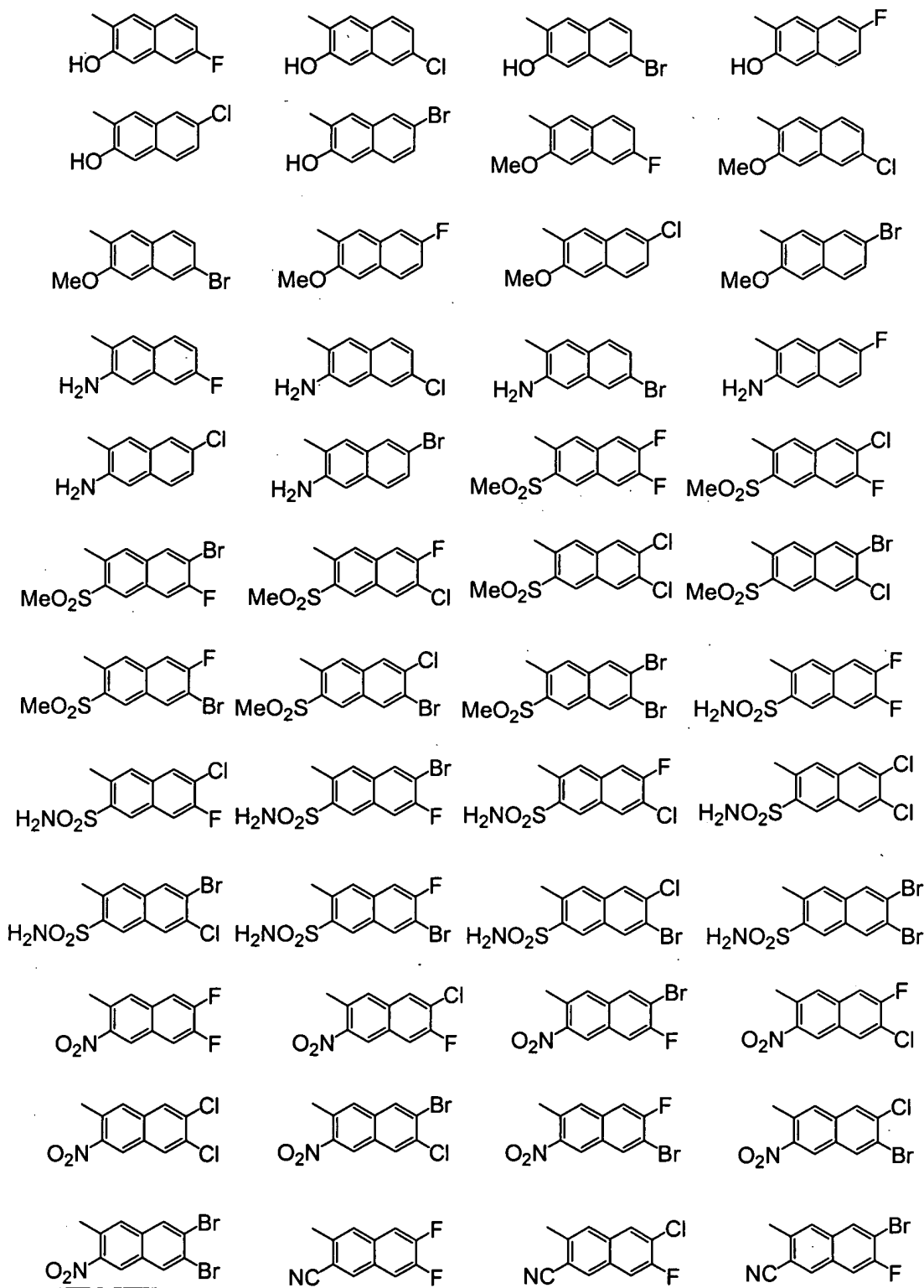
X is selected from the group consisting of:

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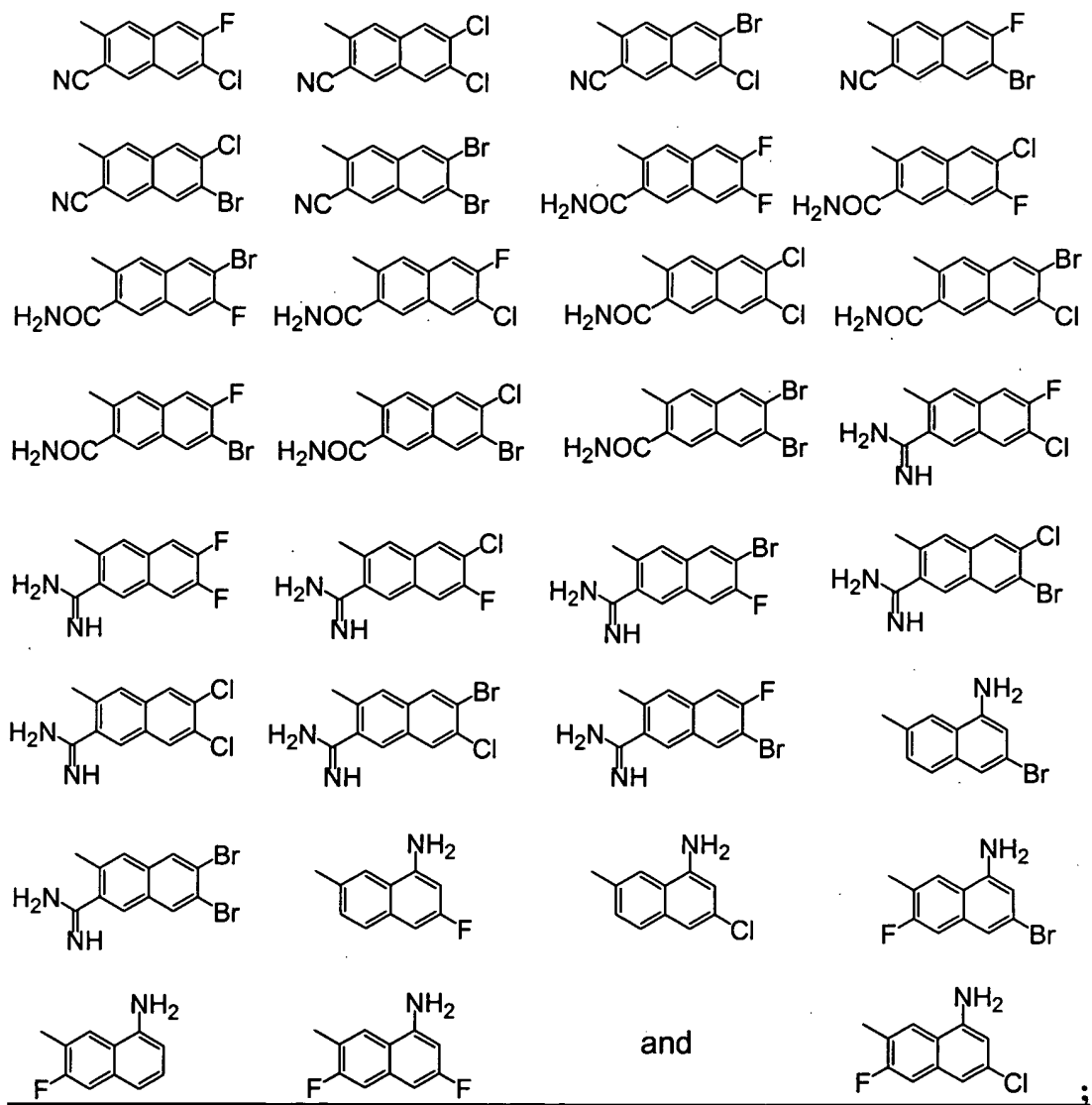


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or all pharmaceutically acceptable diastereomers, enantiomers or mixtures thereof, salts, hydrates or solvates thereof.

31. (Original) The method of claim 30, wherein the condition is selected from the group consisting of:

acute coronary syndrome, myocardial infarction, unstable angina, refractory angina, occlusive coronary thrombus occurring post-thrombolytic therapy or post-coronary angioplasty, a thrombotically mediated cerebrovascular syndrome, embolic stroke, thrombotic stroke, transient ischemic attacks, venous thrombosis, deep venous thrombosis, pulmonary embolus, coagulopathy, disseminated intravascular coagulation,

thrombotic thrombocytopenic purpura, thromboangiitis obliterans, thrombotic disease associated with heparin-induced thrombocytopenia, thrombotic complications associated with extracorporeal circulation, thrombotic complications associated with instrumentation, and thrombotic complications associated with the fitting of prosthetic devices.

32. (Canceled)

33. (Currently amended) A pharmaceutical composition of claim 21 for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising a pharmaceutically acceptable carrier and a pharmaceutically effective amount of a compound of claim 4

wherein:

A is phenyl, which is substituted with 0-2 R¹ groups;

each R¹ is a member independently selected from the group consisting of:

halo, C₁₋₄alkyl, -CN, -C(=O)-N(R², R³), -NO₂, -SO₂N(R², R³), -SO₂R², -(CH₂)_mNR²R³, -(CH₂)_m-C(=NR³)-R², -(CH₂)_m-C(=NR²)-N(R², R³), -(CH₂)_m-N(R²)-C(=NR²)-N(R², R³), -(CH₂)_mNR²-C₃₋₆heterocyclics, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₈cycloalkyl, C₀₋₄alkylC₃₋₈cycloalkyl, -CF₃, -OR², and a 5-6 membered heterocyclic system containing from 1-4 heteroatoms selected from N, O and S;

each R² and R³ is a member independently selected from the group consisting of:

-H, -C₁₋₄alkyl and -C₀₋₄alkyl-(carbocyclic aryl);

m is an integer of 0-2;

Q is a direct link;

D is phenyl, which is substituted with 0-2 R^{1a} groups;

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each R^{1a} is a member independently selected from the group consisting of:

halo, -C₁₋₄alkyl, -CN, -NO₂, -(CH₂)_n-N(-R^{2a}, -R^{3a}), -S(=O)₂-N(-R^{2a}, -R^{3a}), -S(=O)₂-R^{2a}, -CF₃, -(CH₂)_n-OR^{2a}, -C(=O)-O-R^{2a}, -C(=O)-N(-R^{2a}, -R^{3a}), and a 5-6 membered aromatic heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

n is an integer of 0-2;

R^{2a} and R^{3a} are independently selected from the group consisting of:

-H, -C₁₋₄alkyl and -C₁₋₄alkyl-(carbocyclic aryl);

E is -NH-C(=O)-;

G is a pyrazole ring substituted with 0-2 R^{1b} groups;

each R^{1b} is a member independently selected from the group consisting of:

halo, -C₁₋₄alkyl, -CN, -NO₂, -N(-R^{2b}, -R^{3b}), -C(=O)-N(-R^{2b}, -R^{3b}), -S(=O)₂-N(-R^{2b}, -R^{3b}), -S(=O)₂-R^{2b}, -CF₃, -O-R^{2b}, -O-CH₂-CH₂-O-R^{2b}, -O-CH₂-C(=O)-O-R^{2b}, -N(-R^{2b})-CH₂-CH₂-O-R^{2b}, -N(-CH₂-CH₂-O-R^{2b})₂, -N(-R^{2b})-C(=O)-R^{3b}, -N(-R^{2b})-S(=O)₂-R^{3b}, and a 5-6 membered heterocyclic ring containing 1-4 heteroatoms selected from N, O and S;

each R^{2b} and R^{3b} is a member independently selected from the group consisting of:

-H, -C₁₋₄alkyl and -C₁₋₄alkyl-(carbocyclic aryl);

J is a direct link;

X is a naphthyl, which is substituted with 0-3 R^{1c} groups;

each R^{1c} is a member independently selected from the group consisting of:

halo, -C₁₋₄alkyl, -CN, -NO₂, -(CH₂)₂-N(-R^{2c}, -R^{3c}), -C(=O)-N(-R^{2c}, -R^{3c}), -C(=NH)-N(-R^{2c}, -R^{3c}), -C(=NMe)-N(-R^{2c}, -R^{3c}), -S(=O)₂-N(-R^{2c}, -R^{3c}), -S(=O)₂-R^{2c},

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-S(=O)₂-O H, -CF₃, -O-R^{2c}, -O(-CH₂)_z-O-R^{2c}, -O(-CH₂)_z-C(=O)-O-R^{2c}, -N(-R^{2c}),
-O(-CH₂)_z-O-R^{2c}, -N[(-CH₂)_z-O-R^{2c}]₂, -(CH₂)_z-N(-R^{2c})-C(=O)-R^{3c},
-(CH₂)_z-N(-R^{2c})-S(=O)₂-R^{3c}, and a 5-6 membered heterocyclic ring containing 1-4
heteroatoms selected from N, O and S;

z is an integer of 0-4;

each R^{2c} and R^{3c} is a member independently selected from the group consisting of:

-H, -C₁₋₄alkyl and -C₁₋₄alkyl-(carbocyclic aryl);

or all pharmaceutically acceptable diastereomers, enantiomers or mixtures thereof, salts, hydrates or solvates thereof.

26. (Currently amended) ~~The A method for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising administering to said mammal a therapeutically effective amount of a compound of claim 2~~ 22

wherein:

A is phenyl, which is substituted with 0-2 R¹ groups;

each R¹ is a member independently selected from the group consisting of:

halo, -CN, -SO₂N(R², R³), -SO₂R², and -CH₂NR²R³;

each R² and R³ is a member independently selected from the group consisting of:

-H and -C₁₋₄alkyl;

Q is a direct link;

D is phenyl, which is substituted with 0-2 R^{1a} groups;

each R^{1a} is a member independently selected from the group consisting of:

-H and halo;

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E is -NH-C(=O)-;

G is a pyrazole ring substituted with 0-2 R^{1b} groups;

each R^{1b} is a member independently selected from the group consisting of:

- Me, -Et, -CF₃, -C(=O)-NH₂, -NH₂, -NH-(C=O)-Me, -NH-S(=O)₂-Me, -SMe, -S(=O)-Me and halo;

J is a direct link;

X is a naphthyl, which is substituted with 0-3 R^{1c} groups;

each R^{1c} is a member independently selected from the group consisting of:

halo, OH, -OMe, -NH₂, -CN, -NO₂, -CH₂OH, -C₁₋₅alkyl, -C(=O)-N(-R^{2c}, -R^{3c}), -C(=NH)-N(-R^{2c}, -R^{3c}), -S(=O)₂-N(-R^{2c}, -R^{3c}), -S(=O)₂-R^{2c}, -S(=O)₂-OH, -CF₃, 2-imidazolin-2-yl and 1-methyl-2-imidazolin-2-yl;

each R^{2c} and R^{3c} is a member independently selected from the group consisting of:

-H, -OH, -NH₂ and -C₁₋₄alkyl;

or all pharmaceutically acceptable diastereomers, enantiomers or mixtures thereof, salts, hydrates or solvates thereof.

34. (Currently amended) ~~The A method for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising administering to said mammal a therapeutically effective amount of a compound of claim-4~~ 22

wherein:

A is phenyl, which is substituted with 0-2 R¹ groups;

each R¹ is a member independently selected from the group consisting of:

halo, -CN, -SO₂N(R², R³), -SO₂R² and -CH₂NR²R³;

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each R² and R³ is a member independently selected from the group consisting of:

-H and -C₁₋₄alkyl;

Q is a direct link;

D is phenyl, which is substituted with 0-2 R^{1a} groups;

each R^{1a} is a member independently selected from the group consisting of:

-H and halo;

E is -NH-C(=O)-;

G is a pyrazole ring substituted with 0-2 R^{1b} groups;

each R^{1b} is a member independently selected from the group consisting of:

- Me, -Et, -CF₃, -C(=O)-NH₂, -NH₂, -NH-(C=O)-Me, -NH-S(=O)₂-Me, -SMe, -S(=O)-Me and halo;

J is a direct link;

X is a naphthyl, which is substituted with 0-3 R^{1c} groups;

each R^{1c} is a member independently selected from the group consisting of:

halo, OH, -OMe, -NH₂, -CN, -NO₂, -CH₂OH, -C₁₋₅alkyl, -C(=O)-N(-R^{2c}, -R^{3c}), -C(=NH)-N(-R^{2c}, -R^{3c}), -S(=O)₂-N(-R^{2c}, -R^{3c}), -S(=O)₂-R^{2c}, -S(=O)₂-OH, -CF₃, 2-imidazolin-2-yl and 1-methyl-2-imidazolin-2-yl;

each R^{2c} and R^{3c} is a member independently selected from the group consisting of:

-H, -OH, -NH₂ and -C₁₋₄alkyl;

or all pharmaceutically acceptable diastereomers, enantiomers or mixtures thereof, salts, hydrates or solvates thereof.

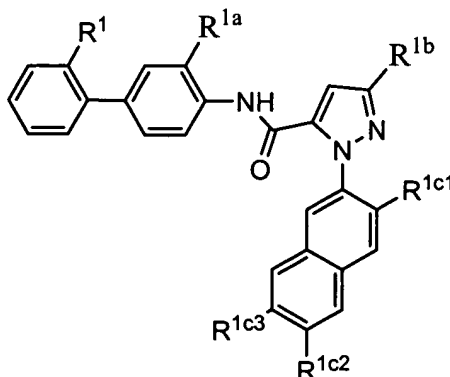
35. (Original) The method of claim 34, wherein the condition is selected from the group consisting of:

acute coronary syndrome, myocardial infarction, unstable angina, refractory angina, occlusive coronary thrombus occurring post-thrombolytic therapy or post-coronary angioplasty, a thrombotically mediated cerebrovascular syndrome, embolic stroke, thrombotic stroke, transient ischemic attacks, venous thrombosis, deep venous thrombosis, pulmonary embolus, coagulopathy, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, thromboangiitis obliterans, thrombotic disease associated with heparin-induced thrombocytopenia, thrombotic complications associated with extracorporeal circulation, thrombotic complications associated with instrumentation, and thrombotic complications associated with the fitting of prosthetic devices.

36. (Canceled)

37. (New) A pharmaceutical composition of claim 21

wherein the compound has the following formula:



R¹ is selected from the group consisting of:

-S(=O)₂-NH₂, -S(=O)₂-Me, -CH₂NH₂, and -CH₂NMe₂;

R^{1a} is selected from the group consisting of:

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-H, -F, -Cl and -Br;

R^{1c1} is independently selected from the group consisting of:

-H, -F, -Cl, -Br, -NH₂, -OH, -SO₂Me, -SO₂Et, -SO₂NH₂, -NO₂, -CN, -CONH₂ and -CH₂OH;

R^{1c2} is independently selected from the group consisting of:

-H, -F, -Cl and -Br;

R^{1c3} is independently selected from the group consisting of:

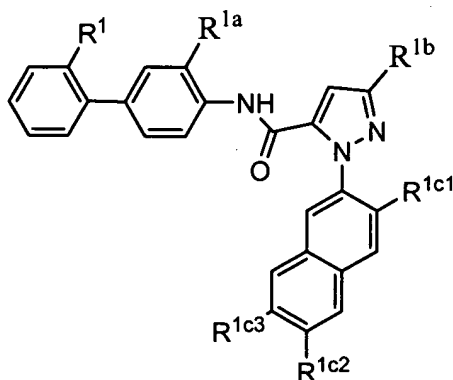
-H, -F, -Cl and -Br;

R^{1b} is selected from the group consisting of:

-H, -CH₃ and -CF₃.

38. (New) The method of claim-22

wherein the compound has the following formula:



R¹ is selected from the group consisting of:

-S(=O)₂-NH₂, -S(=O)₂-Me, -CH₂NH₂, and -CH₂NMe₂;

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R^{1a} is selected from the group consisting of:

-H, -F, -Cl and -Br;

R^{1c1} is independently selected from the group consisting of:

-H, -F, -Cl, -Br, -NH₂, -OH, -SO₂Me, -SO₂Et, -SO₂NH₂, -NO₂, -CN, -CONH₂ and -CH₂OH;

R^{1c2} is independently selected from the group consisting of:

-H, -F, -Cl and -Br;

R^{1c3} is independently selected from the group consisting of:

-H, -F, -Cl and -Br;

R^{1b} is selected from the group consisting of:

-H, -CH₃ and -CF₃.

40. (New) The method of claim 39, wherein the condition is selected from the group consisting of:

acute coronary syndrome, myocardial infarction, unstable angina, refractory angina, occlusive coronary thrombus occurring post-thrombolytic therapy or post-coronary angioplasty, a thrombotically mediated cerebrovascular syndrome, embolic stroke, thrombotic stroke, transient ischemic attacks, venous thrombosis, deep venous thrombosis, pulmonary embolus, coagulopathy, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, thromboangiitis obliterans, thrombotic disease associated with heparin-induced thrombocytopenia, thrombotic complications associated with extracorporeal circulation, thrombotic complications associated with instrumentation, and thrombotic complications associated with the fitting of prosthetic devices.